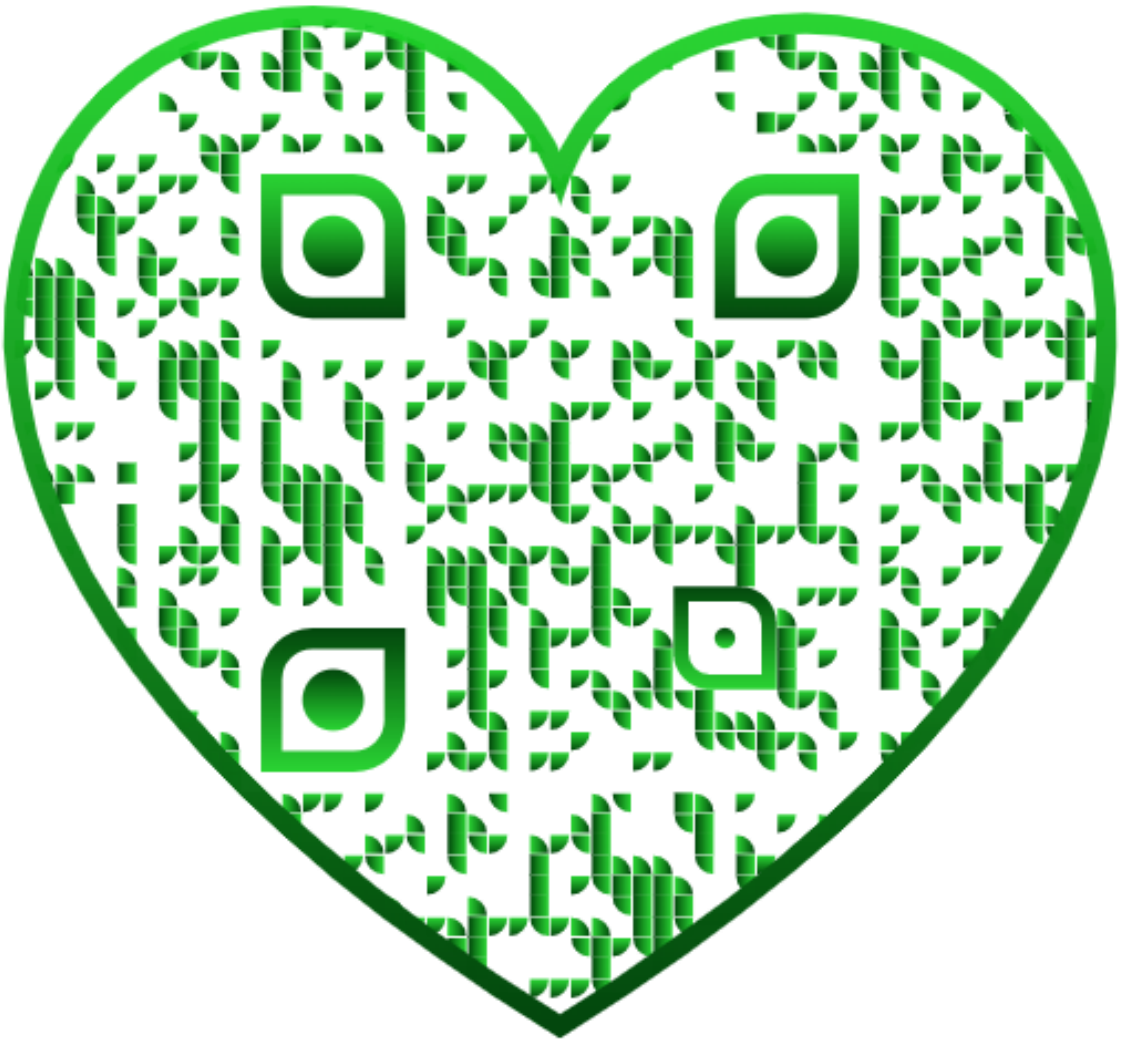
TITRIMETRIC ANALYSIS



Introduction:

- Various methods of Quantitative analysis

1. Chemical methods

a) volumetric methods:

- Assay is based on the measurement of volume of solution of known strength that is required to react completely with the substance to be analyzed.

Depending up on the type of reactions involved:**They are:**

i. **Ion combination reactions:**

- Neutralization titrations
- Precipitation titrations
- Complexometric titration

ii. **Electron transfer reactions:**

- Oxidation reduction titrations

b) Gravimetric methods:

- Gravimetric analysis is a quantitative analysis by weight
- it is a process of isolating and weighing the compound of known composition
- The separation of compound is affected by number of ways like precipitation, volatilization, etc

2. *Instrumental methods*

- Based on the relation between the content and corresponding physicochemical properties of the substance being analyzed.

a) Electrochemical method:

- It measures current, potential, electrical conductivity, etc. with suitable and sensitive instruments.

E.g. Potential – potentiometery.

current - amperometry

b) Chromatographic methods:

- Chromatography is a separation technique or a device by which a mixture of substances is separated into its various components.
- Used for identification & Quantification of different pharmaceuticals.

c) Optical method:

- measures the amount of light absorbed, scattered, emitted or transmitted by the sample solution.

3. Microbiological methods

- Antibiotic sensitivity test
- Microbial limit test
- Sterility test
- Pyrogen test

- Finding a characteristic of the product directly related to its concentration can be achieved by:

- Physical, electrochemical or chromatographic methods.
- These methods are often **costly, require dedicated instruments** and **skilled operators**

- Titrimetric methods are still widely used in pharmaceutical analysis because of their robustness, cheapness and capability for high precision.

- **Titration:** is a volumetric procedure for determining the concentration of an unknown species by adding precisely measured volume of a known species that reacts quantitatively.

- Titrimetric methods are classified into four groups based on the type of reaction involved.

1. **Acid–base titrations:** in which an acidic or basic titrant reacts with an analyte that is a base or an acid;
2. **Complexometric** titrations: involving a metal–ligand complexation reaction;
3. **Redox titrations:** where the titrant is an oxidizing or reducing agent and
4. **Precipitation titrations:** in which the analyte and titrant react to form a precipitate.

- Despite the difference in chemistry, all titrations share several common features.

Common Terminologies:

- ***Titrant:***
  - *The reagent added to a solution containing the analyte and whose volume is the signal.*
- ***Equivalence point:***
  - *The point in a titration where stoichiometrically equivalent amounts of analyte and titrant react.*
- ***End point:***
  - *The point in a titration at which there is a sudden change in a physical property, such as indicator color, pH, conductivity, or absorbance.*
  - *Used as a measure of the equivalence point.*
- ***Indicator:***
  - *A colored compound whose change in color signals the end point of a titration*
- ***Titration error:***
  - *The determinate error in a titration due to the difference between the end point and the equivalence point.*

Strength and limitation of titration method:

- **Advantages**
  - Capable of a higher degree of precision and accuracy than instrumental methods of analysis, with precisions of +/- 0.1% being achieved,
  - The methods are generally robust,
  - Analyses can be automated,
  - Cheap to perform and do not require specialized apparatus and
  - They are absolute methods and are not dependent on the calibration of an instrument
- **Limitations**
  - Non-selective,
  - Time-consuming if not automated and require a greater level of operator skill than routine instrumental methods,
  - Require large amounts of sample and reagents and
  - Reactions of standard solutions with the analyte should be rapid and complete

Requirements for Volumetric Methods:

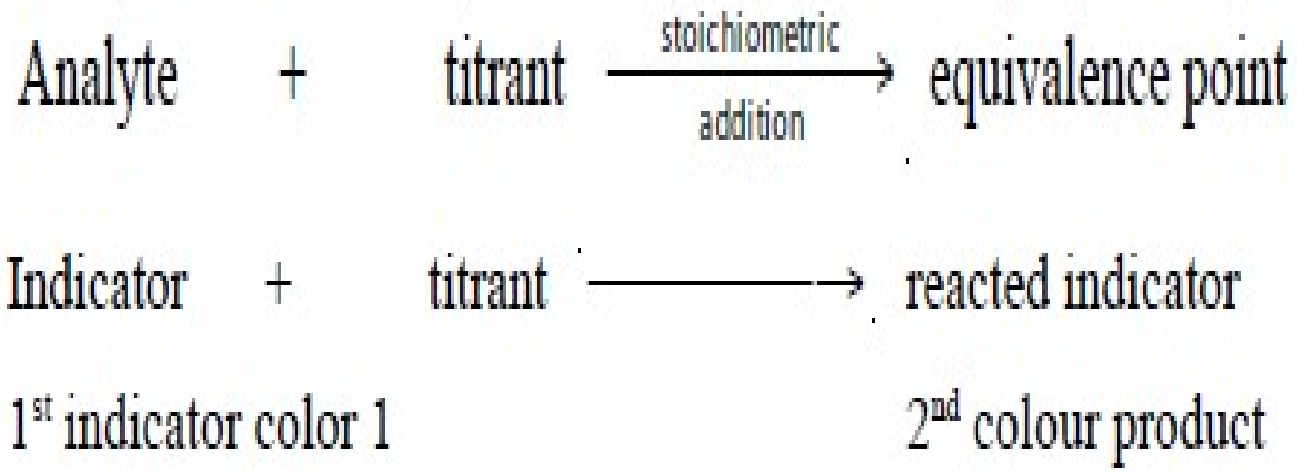
- For use of chemical reaction in volumetric methods, the reaction should fulfill some of the requirements:
  - ✓ The titrant should either be a standard or should be standardized,
  - ✓ The reaction must proceed by a definite chemistry,
  - ✓ The reaction should be nearly complete at the equivalence point.,
  - ✓ The reaction rate should be fast enough to be practical.

- These are significant limitations and, for this reason, several titration strategies are commonly used.

Principles of titration

Titration

- ✓ A procedure in which one substance (titrant) is carefully added to another (analyte) until complete reaction has occurred.
- ✓ The quantity of titrant required for complete reaction tells **how much analyte** is present.



Basic calculations:

In quantitative procedures:

- Measuring the **amount of reagent of known concentration** that is consumed by the **analyte**. i.e $\mathbf{V_t}$
- knowledge of the **stoichiometry of the reaction** b/n the titrant and the analyte(s) is basic one.

$$n_A\,\mathbf{A} + n_T\,\mathbf{T} \rightarrow \mathbf{products;}$$

Where A and T represent the analyte and titrant, respectively, and n_A and n_T are the stoichiometric coefficients

At the equivalent point

No of mole of analyte = No of mole of titrant

$$\frac{M_A \times V_A}{n_A} = \frac{M_T \times V_T}{n_T}$$

Where A and T represent the analyte and titrant, respectively, and n_A and n_T are the stoichiometric coefficients.

Titration Procedures (Direct and indirect(back))

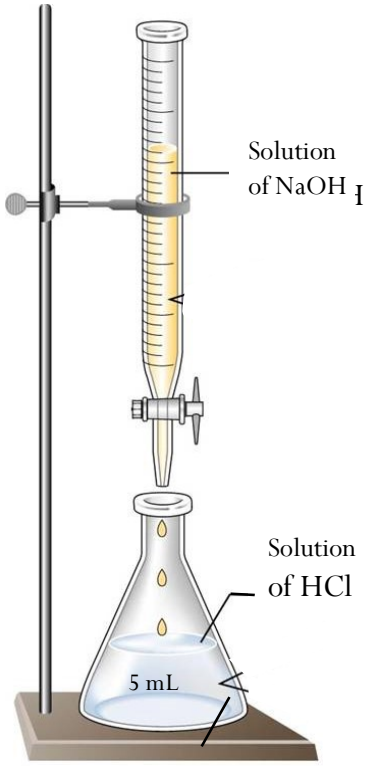
The specific titration procedure depends on the nature of the substance

Direct Titration

- One in which the analyte is treated with titrant, and the volume of titrant required for complete reaction is measured.
  - The analyte is directly involved in the titration reaction.
- titrant + analyte ⟶ product(s)

$(NaOH) + (HCl) \longrightarrow Na^+Cl^- + H_2O$

At equivalent point:
moles H_3O^+ = moles OH^-
M*V/ n = M*V/ n



- **Direct titrations calculations**
  - A 25.0 mL sample of HCl is titrated with 37.31 mL of 0.5119 M NaOH. What is the molarity of the HCl in the sample?

    HCl + NaOH ↔ H_2O + NaCl

  - Moles NaOH = 0.5119 moles/L x 37.31 mL x 1L/1000mL

    At the equivalent point:

    Moles HCl = moles NaOH = 0.01910 moles

    M_{HCl} = moles/volume = 0.01910 moles/0.0250 L = 0.7618 M

    (Q) 42.5 mL of 1.3M KOH are required to neutralize 50.0 mL of $H_2SO_4^-$. Find the molarity of H_2SO_4.

Back Titration

- One in which an excess of standard reagent is added to react with analyte. Then the unreacted excess reagent is titrated with a second reagent or with a standard solution of analyte.

Analyte + reagent ↔ product(s) + reagent remaining

Titrant + reagent remaining ↔ product(s)

- Back titration is used due to:
  - **Insoluble substances. E.g. Li_2CO_3, $CaCO_3$**
  - **When the reaction between analyte and titrant is very slow.**
  - **Volatile solutions,**

    e.g. ammonia, some of which is lost during the direct titration
  - **Substances for which quantitative rxn proceeds rapidly only in presence of excess of the reagent.**

- **Back Titration Calculation-**

✓ Antacids, which are bases, are reacted with excess acid and this excess acid is titrated with standard base.

Antacid + HCl (initial) ↔ neutralized antacid + HCl (leftover)

HCl (leftover) + **NaOH** ↔ NaCl + H2O

moles HCl initially = M_{HCl} x V_{HCl}

moles HCl left-over = moles NaOH = M_{NaOH} x V_{NaOH}

mole HCl reacted = moles HCl initially - moles HCl left-over

 # mole of antiacid = # mole of HCl reacted

Titration Curves

- A graph showing the progress of titration as a function of the volume of titrant added.
- It is a graph of **'-log [H+]** as a function of **titrant-volume.**

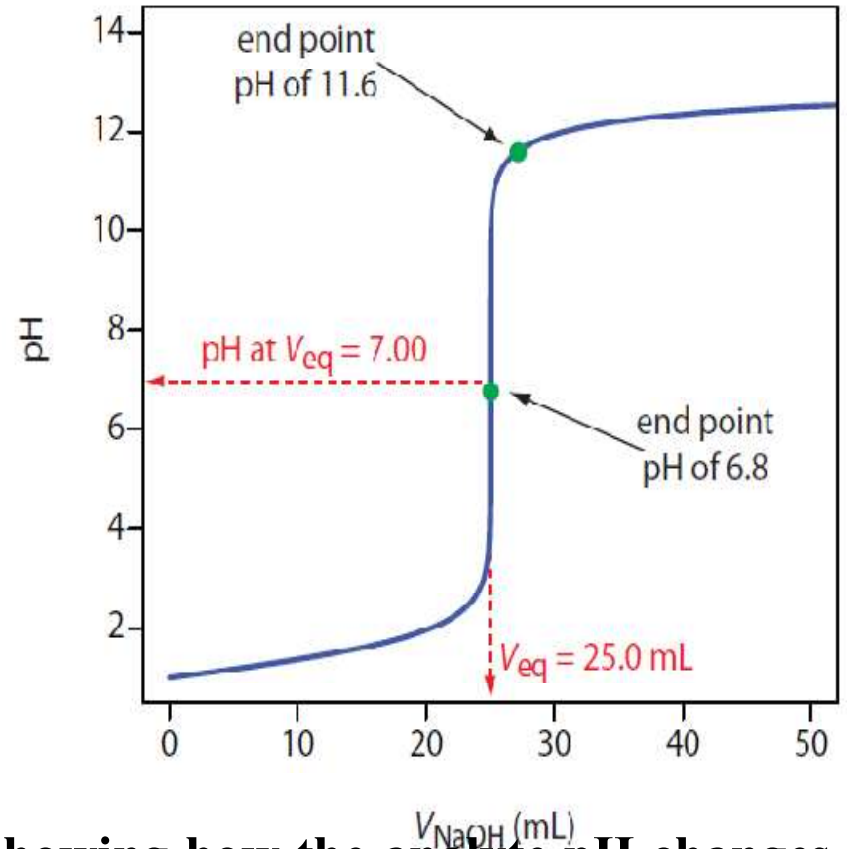


Figure: Typical acid–base titration curve showing how the analyte pH changes with the addition of titrant. The analyte is a 25.0 mL solution of 0.100 M HCl and the titrant is 0.100 M NaOH.

- Acid- base titration is a **neutralization titrations**

1. **Aqueous acid-base titrations :** It involves neutralization reaction in presence of water as solvent.
2. **Non-aqueous titrations:** It involves the reaction between acid and base in presence of non-aqueous medium i.e. organic solvents.

- For an acid–base titration, the equivalence point is characterized by **a pH level** that is a function of the acid–base strengths and concentrations of the analyte and titrant.

- The pH at the end point, however, may or may not correspond to the pH at the equivalence point.

1. Aqueous acid-base titrations

❖Titrating Strong Acids by Strong Bases

- In the titration of 50.0 mL of 0.100 M HCl with 0.200 M NaOH,

a) What is the equivalence volume in mL?

b) After adding10.0 mL of NaOH, what is the pH of the solution?

c) After adding 30.0 mL of NaOH, what is the pH of the solution?

For the reaction of a strong base with a strong acid the only important equilibrium reaction is

$$H_3O^+(aq) + OH^-(aq) \rightleftharpoons 2H_2O(\ell)$$

▪At the equivalence point we know from the reaction:

$$\text{Moles HCl} = \text{moles NaOH}$$

$$M_a V_a = M_b V_b$$

$$V_{eq} = V_b = \frac{M_a V_a}{M_b} = \frac{(0.100\ \text{M})(50.0\ \text{mL})}{(0.200\ \text{M})} = 25.0\ \text{mL}$$

b) After adding10.0 mL of NaOH…pH?

- Before the equivalence point, HCl is present in excess and the pH is determined by the concentration of **excess HCl**
  - ➢ therefore, the concentration of excess HCl is

$$[HCl] = \frac{\text{moles excess HCl}}{\text{total volume}} = \frac{M_a V_a - M_b V_b}{V_a + V_b}$$

$$= \frac{(0.100\ M)(50.0\ mL) - (0.200\ M)(10.0\ mL)}{50.0\ mL + 10.0\ mL} = 0.050\ M$$

$$pH = -\log [0.05] = \underline{\mathbf{1.30}}$$

c) After adding 30 mL of NaOH…pH?

- After the equivalence point, **OH^-** is present in excess and the pH is determined by:

$$[OH^-] = \frac{\text{moles excess NaOH}}{\text{total volume}} = \frac{M_b V_b - M_a V_a}{V_a + V_b}$$

$$= \frac{(0.200\ \text{M})(30.0\ \text{mL}) - (0.100\ \text{M})(50.0\ \text{mL})}{50.0\ \text{mL} + 30.0\ \text{mL}} = 0.0125\ \text{M}$$

To find the concentration of H_3O^+, we use the K_w expression

$$[H_3O^+] = \frac{K_w}{[OH^-]} = \frac{1.00 \times 10^{-14}}{0.0125} = 8.00 \times 10^{-13}$$

OR:

$pOH = -\log [OH^-]$

$pOH + pH = 14$

$pH = 14 - pOH$

12.10

❖Titrating a Weak Acid with a Strong Base

- For example, let's consider the titration of 50.0 mL of 0.100 M acetic acid (CH3COOH) with 0.100 M NaOH.
  a) What is the equivalence volume in mL?
  b) What was the pH before titration?

$$\text{Moles } CH_3COOH = \text{moles NaOH}$$

$$M_aV_a = M_bV_b$$

$$V_{eq} = V_b = \frac{M_aV_a}{M_b} = \frac{(0.100\ M)(50.0\ mL)}{(0.100\ M)} = 50.0\ mL$$

b) Before adding any NaOH the pH is that for a solution of 0.100 M acetic acid.

➢Since acetic acid is a weak acid, we can calculate the pH based on its dissociation constant:

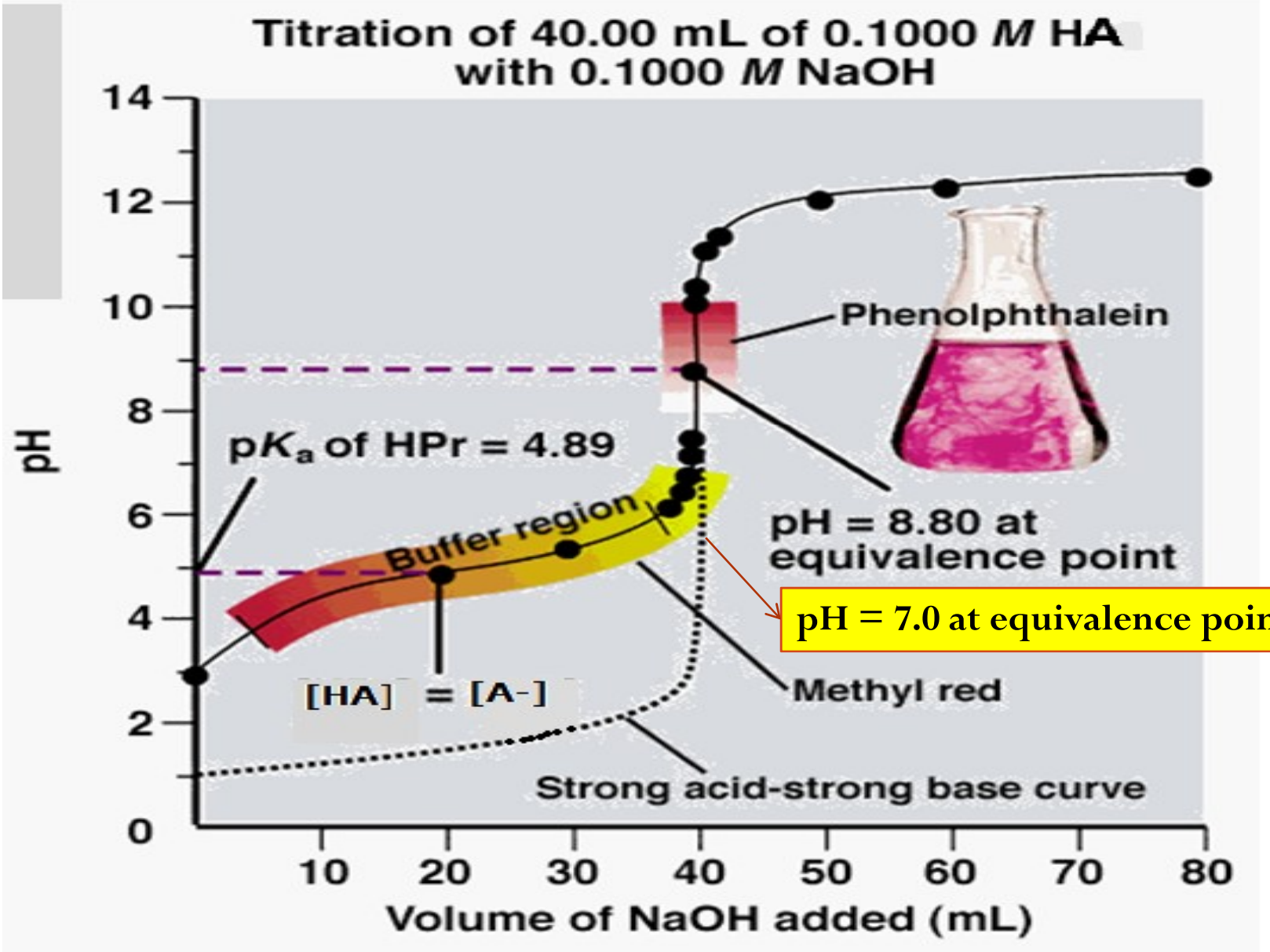
$$CH_3COOH(aq) + H_2O(\ell) \rightleftharpoons H_3O^+(aq) + CH_3COO^-(aq)$$

$$K_a = \frac{[H_3O^+][CH_3COO^-]}{[CH_3COOH]} = \frac{(x)(x)}{0.100 - x} = 1.75 \times 10^{-5}$$

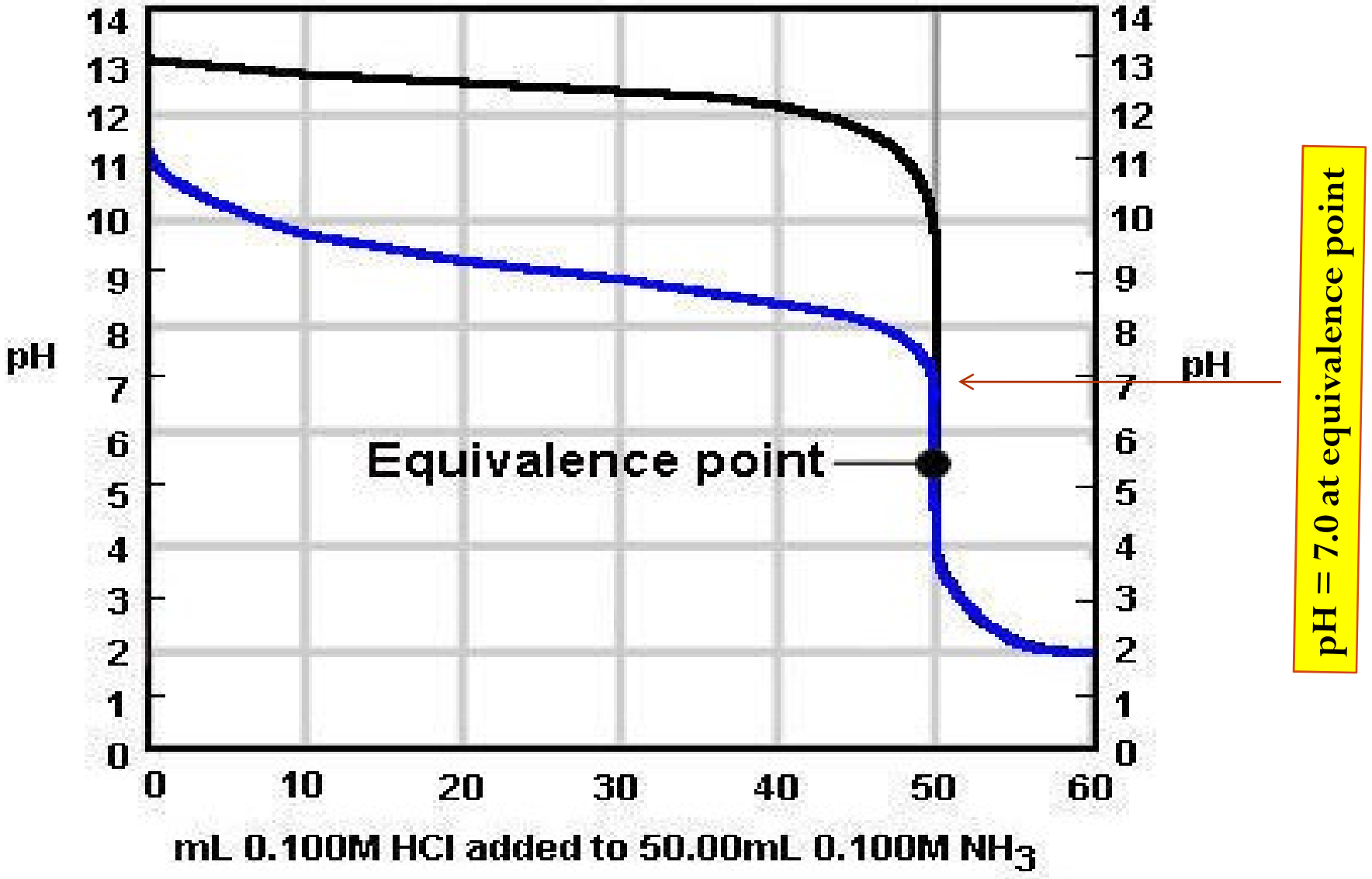
$$x = [H_3O^+] = 1.32 \times 10^{-3}$$

$$pH = -\log[X] = 2.88$$

Titration curves of SA with SB and WA with SB



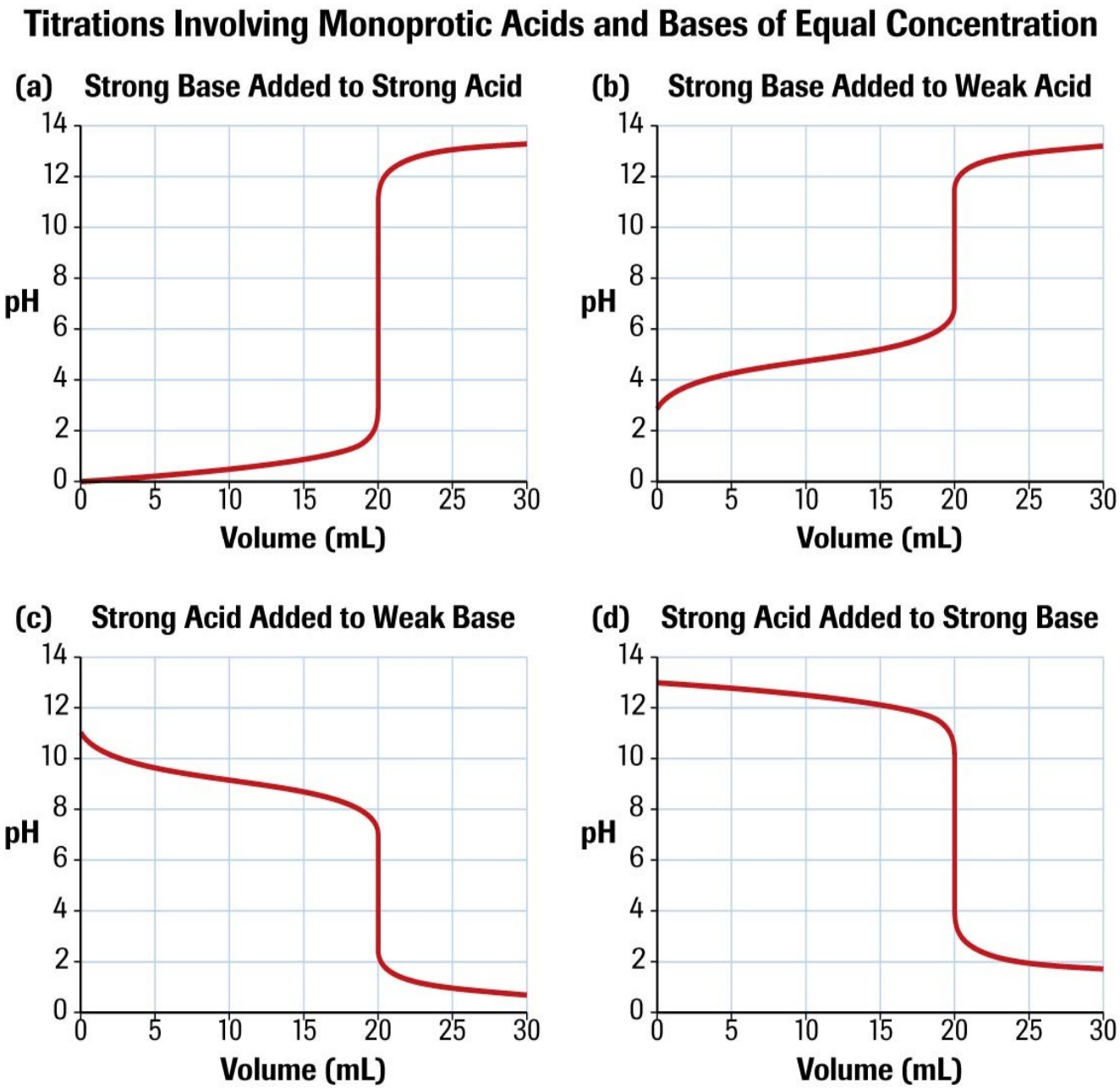
Titration curves of SB with SA and WB with SA



General Rule

Strong Acid to Weak Base: pH at equivalence point is always lower than 7

Strong Base to Weak Acid: pH at equivalence point is always higher than 7



Equivalent point detection

- Equivalence point is theoretical value at which mole of the titrant is equal to mole of the titrand.
  - For each H ion consumption, there will be one equivalence point.
  - Ex. For triprotic weak acid (H_3PO_4) there will be 3 eq. points.
- Eq. point can be estimated (detected) form the titration curve
  - The most inflection points, corresponding to the greatest slope is nearly the equivalence point.
  - Eg in SB/SA titration

Limitations:

- Eq. points sometimes may be missing (difficult to detect).
  - Ex. Weak Acid (**Ka < 10^{-9}**)
  - Meltiprotic acids (**▲ pKa at least 2.7**)

End point detection

- End point is the experimental value that can best estimate the eq. point
- The main object of end point detection is to **find out the volume of standard solution**, which reacts with the analyte completely.
- In volumetric methods, the end point is usually detected by use of some **external substance**, which shows sharp change in its color at the end point of the reactions.
  - This external substance, which detects the end point, is called a **visual indicator.**

End point detection by Acid base Indicators

- **Indicator:**
  - a substance which exhibit colour change at a particular stage of a chemical reaction or compounds whose colors are **sensitive to pH.**
  - Enable eye to estimate the ***end point of a titration***
  - Acid - base indicators are usually an organic dyes that itself **a weak acid or base:**

$$\underset{\text{Color 1}}{HInd\,(aq)} + H_2O\,(l) \rightleftharpoons H_3O^+\,(aq) + \underset{\text{Color 2}}{Ind^-\,(aq)}$$

$$K_a \text{ for the indicator} = \frac{[H_3O^+][Ind^-]}{[HInd]}.$$

Taking the negative log of each side and rearrange the equation:

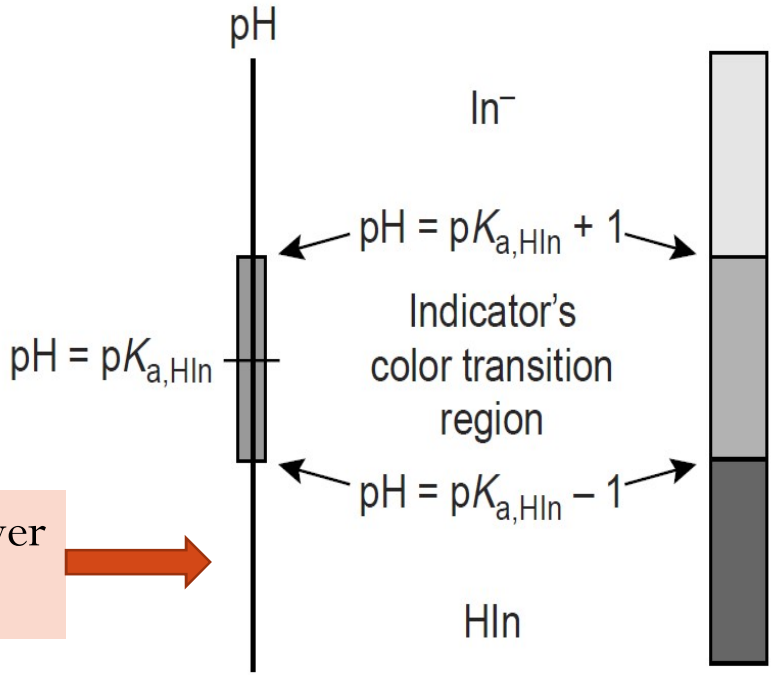
$$pH = pK_a + \log\frac{[In^-]}{[HIn]}$$

- If we assume that both HIn and In– can be detected with equal easy;
- The transition b/n two colors reaches its mid point when:
  - pKa HIn = pH of the equivalence point.

  - **Ex** : if HIn is **red** and In- is yellow, then
    - At medium pH in which [HIn] = [In^-] **orange can be observed.**
- In this case, the equivalence point coincides with the end point.
- **Challenges:**
  - Exact pH at equivalence point is rarely known
  - Color change may be subtle

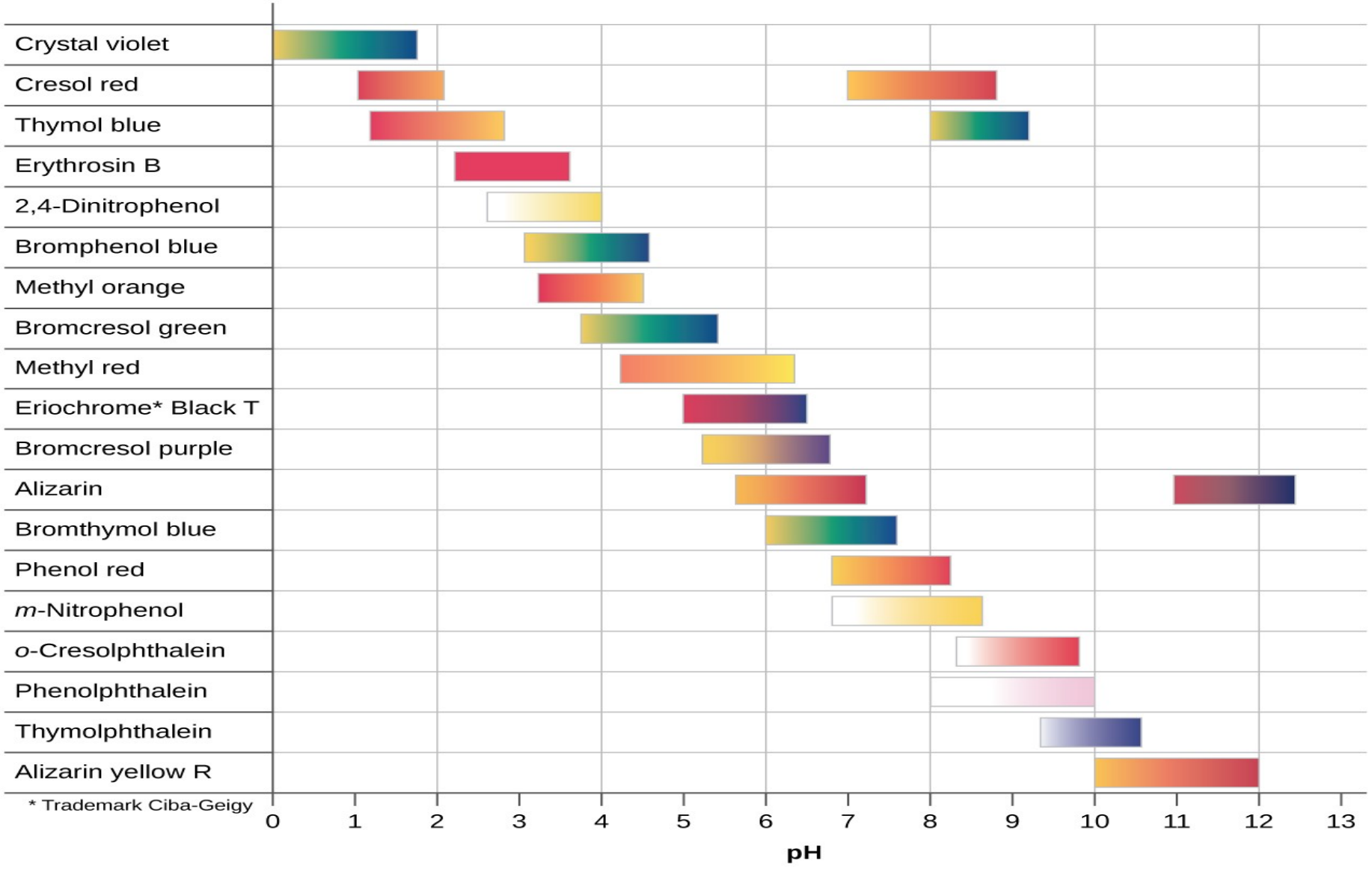
- A range of pHs over which the average analyst will observe a change in color is established by assuming that the color of solution is the color of HIn whenever [HIn] = 10[In^-] and vise versa.
- The previous example, can be explained in this case:
  - At low pH in which [HIn] is dominant, the ratio of 10/1 (**red**).
  - At high pH in which [In^-] is dominant, the ratio of 1/10 (**yellow**).

The Color change will appear in the range of **pKa**HIn ± **1** i.e. over approximately **2 pH unit.**



Ladder diagram showing the range of pH levels over which a typical acid-base indicator changes color.

❖*This chart illustrates the ranges of color change for several acid-base indicators:*



Properties of an indicators

- Indicators must have the following properties :
  - The indicator must change color as **close to the equivalence point** with the addition of one drop of solution from the burette.
  - The indicator should have **high color intensity** to use in small amount.
  - The first color change should be **distinct or Sharp**.
  - Indicator **should not be effect by change in Temperature**.

General procedures

Visual Titration

- *An aliquot of the drug solution was measured accurately and transferred into a clean titration flask and the total volume was brought with appropriate solvent.*
- *Then, 2 to 4 drops of the required indicator are added and the solution is titrated with standard titrant solution to end point.*

➢ Weak acids are titrated in the presence of indicators which change under slightly alkaline conditions.

➢ Weak bases should be titrated in the presence of indicators which change under slightly acidic conditions.

- *A blank titration was performed and necessary volume corrections were made.*
- *The amount of the drug can be calculated:*

Applications

- **Ex-1:** The company recently received a shipment of salicylic acid, $C_7H_6O_3$, to be used in the production of acetylsalicylic acid (aspirin). The shipment can be accepted only if the salicylic acid is more than 99% pure. To evaluate the shipment's purity, a 0.4208-g sample is dissolved in water and titrated to the phenolphthalein end point, requiring 21.92 mL of 0.1354 M NaOH. Salicylic acid is a diprotic weak acid with p*Ka values of 2.97 and 13.74.*
- **Request:** Report the shipment's purity as %w/w $C_7H_6O_3$; (Is it Accepted or rejected?)

Solution

- Because salicylic acid is a diprotic weak acid, the titration, therefore, is to the first equivalence point for which the moles of NaOH equal the moles of salicylic acid; thus

$$\frac{0.1354 \text{ mol NaOH}}{\text{L}} \times 0.02192 \text{ L} = 2.968 \times 10^{-3} \text{ mol NaOH}$$

$$2.968 \times 10^{-3} \text{ mol NaOH} \times \frac{1 \text{ mol } C_7H_6O_3}{\text{mol NaOH}} \times \frac{138.12 \text{ g } C_7H_6O_3}{\text{mol } C_7H_6O_3} = 0.4099 \text{ g } C_7H_6O_3$$

$$\frac{0.4099 \text{ g } C_7H_6O_3}{0.4208 \text{ g sample}} \times 100 = 97.41\% \text{ w/w } C_7H_6O_3$$

Because the purity of the sample is less than 99%, we reject the shipment.

- **Ex-2:** Limestone consists mainly of CaCO3, with traces of iron oxides and other metal oxides. To determine the purity of a limestone, a 0.5413-g sample is dissolved using 10.00 mL of 1.396 M HCl. After heating to expel CO_2, the excess HCl was titrated to the phenolphthalein end point, requiring 39.96 mL of 0.1004 M NaOH.
- **Request:** Report the sample's purity as %w/w CaCO3?

Solution

The total moles of HCl used in this analysis is

$$\frac{1.396 \text{ mol NaOH}}{\text{L}} \times 0.01000 \text{ L} = 1.396 \times 10^{-2} \text{ mol HCl}$$

Of this,

$$\frac{0.1004 \text{ mol NaOH}}{\text{L}} \times 0.03996 \text{ L} \times \frac{1 \text{ mol HCl}}{\text{mol NaOH}} = 4.012 \times 10^{-3} \text{ mol HCl}$$

are consumed in the back titration with NaOH, which means that

$$1.396 \times 10^{-2} \text{ mol HCl} - 4.012 \times 10^{-3} \text{ mol HCl} = 9.95 \times 10^{-3} \text{ mol HCl}$$

react with the $CaCO_3$. Because CO_3^{2-} is dibasic, each mole of $CaCO_3$ consumes two moles of HCl; thus

$$9.95 \times 10^{-3} \text{ mol HCl} \times \frac{1 \text{ mol } CaCO_3}{2 \text{ mol HCl}} \times \frac{100.09 \text{ g } CaCO_3}{\text{mol } CaCO_3} = 0.498 \text{ g } CaCO_3$$

$$\frac{0.498 \text{ g } CaCO_3}{0.5143 \text{ g sample}} \times 100 = 96.8\% \text{ w/w } CaCO_3$$

The end of aqueous acid- base titration!